

Physiology of the Female Reproductive System (1)

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ILOs

By the end of this lecture the student should be able to:

- Explain the physiologic changes that occur in the female reproductive organs during the menstrual cycle (ovarian cycle - uterine cycle).
- Name the key hormones secreted by graafian follicles and corpora lutea of the ovaries.
- Define anovulatory cycles

Function of female reproductive system

- Production of ova (Oogenesis)
- Reception of sperm
- Maintenance of developing fetus (pregnancy)
- Giving birth to baby and lactation

Function of ovaries

- Oogenesis (production of ova)
- Secretion of estrogen and progesterone

Oogenesis

- In humans, no new ova are formed after birth.
- During fetal development, the primitive germ cells called oogonia divide by mitosis into immature ova called primary oocyte. Each primary oocyte becomes surrounded by a single layer of granulosa cells forming a primordial follicle. During fetal development, the ovaries contain over 7 million primordial follicles.
- However, many undergo atresia (involution) before birth and others are lost after birth.

- At the time of birth, there are 2 million ova, but 50% of these are atretic. The million that are normal undergo the first part of the first meiotic division but are arrested and the ova remain in this condition till puberty. However, follicular atresia continues and the number of ova in both of the ovaries at the time of puberty is less than 300,000. Only one of these ova per cycle (or about 500 in the course of a normal reproductive life) normally reaches maturity; the remainder degenerate.
- Just before ovulation, the first meiotic division is completed. One of the daughter cells, the secondary oocyte, receives most of the cytoplasm, while the other, the first polar body, fragments and disappears.
- The secondary oocyte immediately begins the second meiotic division, but this division stops and is completed only when a sperm penetrates the oocyte. At that time, the second polar body is expelled and the fertilized ovum proceeds to form a new individual (fetus).

Menstrual Cycle

- Female reproductive system shows regular cyclic changes which are periodic preparations for fertilization and pregnancy. The cycle is called menstrual cycle.
- Most obvious is periodic vaginal bleeding that occurs with the shedding of the uterine mucosa (menstruation).
- Length of cycle is variable in women, but an average is 28 days from the start of one menstrual period to the start of the next.
- The menstrual cycle involves cyclic changes in 2 organs: the ovary (the ovarian cycle) and the uterus (the endometrial cycle).

Ovarian Cycle

- It starts after onset of puberty
- Normally lasts in average 28 days
- Is interrupted by pregnancy
- Is terminated by menopause

The ovarian cycle consists of the following 2 phases:

- The follicular phase
- The luteal phase

The follicular phase

- It occurs in the first half of the cycle (first 14 days)
- At the start of each cycle, under the influence of follicle stimulating hormone (FSH), several primordial follicles enlarge and a cavity forms around the ovum (antrum formation) and the follicle is now called antral or secondary follicle, capable of estrogen secretion. This cavity is filled with follicular fluid which originates partially from transudation of plasma and partially from follicular cell secretion.
- The shift to an antral follicle initiates rapid follicular growth. During this time, the ovum itself also enlarges and the follicle increases in size. Part of the follicular growth is the result of continued proliferation of the granulosa and theca cells, but most results from a dramatic expansion of the antrum. As the follicle grows, estrogen is produced in increasing quantities.
- On about the 6th day, usually one of the follicles in one ovary starts to grow rapidly and becomes the dominant follicle (graafian follicle), while the others regress, forming atretic follicles. It is uncertain how one follicle is selected to be the dominant follicle in this follicular phase of the menstrual cycle, but it seems to be related to the ability of the follicle to secrete the estrogen inside it that is needed for final maturation.
- The primary source of circulating estrogen is the granulosa cells of the ovaries; however, the cells of the theca interna of the follicle are necessary for the production of estrogen as they secrete androgens that are aromatized to estrogen by the granulosa cells.
- Near midcycle (at about the 14th day), estrogen secretion from the follicle is excessively raised and the markedly increased plasma estrogen level through a +ve feedback mechanism triggers a burst of luteinizing hormone (LH) secretion called LH surge (probably by augmenting the response of anterior pituitary gland to GnRH).
- Such LH surge causes full maturation of the follicle then ovulation which occurs about 9 h after the LH peak.
- The process of ovulation is rupture of the mature graafian follicle and release of the ovum which is extruded into the abdominal cavity. The ovum is picked up by the fimbriated ends of the uterine tubes (oviducts) and either:
 - If the ovum is fertilized, it is transported to the uterus
 - If not fertilized, it will be lost out through the vagina during menstruation.

The luteal phase

- It occupies the second half of the cycle (last 14 days)
- The follicle that ruptures at the time of ovulation is filled with blood, forming a corpus hemorrhagicum. Minor bleeding from the follicle into the abdominal cavity may cause peritoneal irritation leading to lower abdominal pain. The granulosa and theca cells of the follicle begin to proliferate, and the clotted blood is rapidly replaced with yellowish, lipid rich luteal cells, forming the corpus luteum. The luteal cells secrete progesterone and estrogen.
- The corpus luteum continues to grow and reaches full maturation on about the 21st day of the cycle and its hormones prepare the uterine endometrium for implantation of the ovum (if fertilized).
 - If pregnancy (fertilization and implantation) occurs, the corpus luteum persists and continues to secrete its hormones and is called corpus luteum of pregnancy.
 - If pregnancy does not occur, the corpus luteum begins to degenerate about 4 days before the next menses (24th day of the cycle) and is replaced by scar tissue, forming a corpus albicans.

Uterine Cycle (Endometrial Cycle)

- These are cyclic changes in uterus due to changes in levels of estrogen and progesterone during ovarian cycle.
- Its duration averages 28 days
- It prepares uterus for implantation of fertilized ovum and maintenance of early developing embryo.
- It consists of 3 phases:
 - Proliferative phase
 - Secretory phase
 - Menstrual phase

Proliferative phase (preovulatory or follicular phase)

- It coincides with last portion of follicular phase.
- It lasts from end of menstrual phase to beginning of ovulation
- It is under the influence of estrogen secreted by newly growing follicles.
- Estrogen stimulates proliferation of epithelial cells, glands, and blood vessels in the endometrium, thus endometrium increases rapidly in thickness. The uterine glands increase in length but they do not secrete.

- The high estrogen levels trigger the LH surge responsible for ovulation.

Secretory phase (luteal phase)

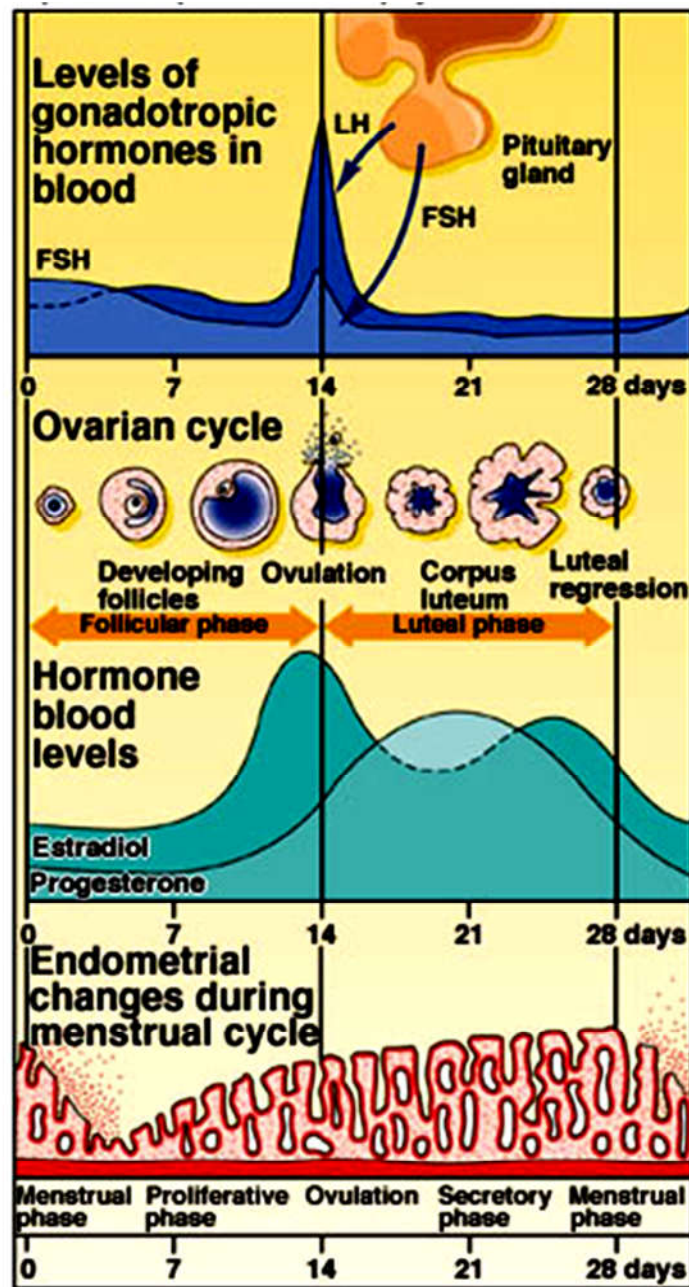
- It coincides with the ovarian luteal phase, after ovulation has occurred.
- It is under the influence of progesterone and estrogen secreted by corpus luteum.
- Estrogen causes slight additional cellular proliferation in the endometrium.
- Progesterone causes the endometrium to become more highly vascularized and slightly edematous. The endometrial glands become coiled and tortuous, secrete a clear fluid and are storing glycogen for early nourishment of a developing embryo before it implants.
- The secretory phase prepares the uterus for implantation of a fertilized ovum and supporting an early embryo after implantation.

Menstrual phase (Menstruation)

- It coincides with end of ovarian luteal phase and onset of new follicular phase.
- The first day of menstruation is start of new ovarian cycle.
- It is characterized by discharge of blood and endometrial debris from vagina 2 days after involution of corpus luteum.
- Menstruation is caused by:

Sharp drop in levels of progesterone and estrogen as the corpus luteum degenerates resulting in:

- Deprivation of the endometrium from hormonal support so it involutes and decreases in thickness.
- Release of uterine prostaglandin that causes:
 - i. vasoconstriction of the endometrial vessels causes necrosis of endometrium. The entire uterine lining sloughs except a deep thin layer of epithelial cells and glands from which new endometrium will regenerate.
 - ii. contractions of the uterine myometrium to expel the blood and endometrial debris from the uterine cavity out through the vagina as menstrual flow.



Menstrual Cycle

Normal Menstruation

- Menstrual blood is predominantly arterial, and only 25% of the blood is venous.
- It contains tissue debris, prostaglandins, and relatively large amounts of fibrinolysin from endometrial tissue.
- Blood in the menstrual flow usually does not clot because the fibrinolysin lyses clots. Only when the flow is excessive blood clots may appear because it may not have sufficient time to be exposed to fibrinolysin.
- Large numbers of leukocytes are found in the menstrual flow which has an important defense role in helping the raw endometrium to resist infection.
- The usual duration of the menstrual flow is 3–5 days, but flows as short as 1 day and as long as 8 days can occur in normal women.
- The amount of blood lost may range normally from slight spotting to 80 mL, the average amount lost is 30 mL. Loss of more than 80 mL is abnormal.

Dysmenorrhea (Painful menstruation)

It is the menstrual cramps due to excessive uterine contractions caused by prostaglandin overproduction

Anovulatory Cycles

- These are menstrual cycles without ovulation due to insufficient LH surge.
- Anovulatory cycles are common for the first 12–18 months after the onset of puberty and also before the onset of the menopause.
- When ovulation does not occur, no corpus luteum is formed and no secretion of progesterone and the effects of progesterone on the endometrium are absent.
- Estrogens continue to cause growth of the endometrium, and the proliferative endometrium becomes thick enough to break down and begins to slough causing bleeding.
- The menstrual cycles are shorter than normal and cannot lead to pregnancy).
- The flow is also variable.